Mycosis Fungoides

Topical Use of Nitrogen Mustard in Recurrent Cases

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■ *The management of the patient with mycosis fungoides requires a variety of therapeutic modalities depending on the stage of the disease. Topically applied nitrogen mustard in the early stages of the disease has a beneficital palliative effect. The effects of nitrogen mustard paintings in the later course of the disease have not been previously reported. In the present study, topically applied nitrogen mustard solution was used to control recurrences of mycosis fungoides following electron beam therapy in 11 patients. Each patient received whole body applications of freshly prepared 10 mg per 50 ml solution of mechlorethamine hydrochloride (a nitrogen mustard) in water daily for seven days. In all patients pruritus disappeared within the first week and ulcers and plaques improved or disappeared in two to four weeks. The seven-day courses of mechlorethamine paintings were repeated as recurrences were noted. Mycosis fungoides was controlled by this therapy for periods ranging up to 15 months.*

Absence of systemic toxicity, a low incidence of cutaneous irritation and application of the treatments at home make topical nitrogen mustard a useful adjunct in the management of the late stages of mycosis fungoides.

THE SUPPRESSIVE EFFECT of topical applications of nitrogen mustard in the early eczematous and plaque stages of mycosis fungoides has been well documented since its introduction by Haserick, Richardson and Grant in 1959.[1-4] The later stages require extensive superficial roentgen therapy or high-energy electron beam therapy.[5]

Patients with mycosis fungoides who have recurrences after x-ray or electron beam therapy pose a therapeutic problem for dermatologists. Anti-metabolities and alkylating agents are effective palliative agents but undesirable systemic toxicity accompanies their use.

The present study describes the effect of topically applied nitrogen mustard in patients with mycosis fungoides in relapse who had previously received electron beam therapy.

Method

The patient's skin is cleansed of all lotions and ointments by a soap and water bath. The physician (or a specially trained relative of the patient) wears rubber gloves while mixing and applying

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the solution. The necessary equipment consists of a 50 ml medicine cup, a 10 ml syringe and 22 gauge needle, gauze squares, a hemostat, room temperature tap water and a 10 mg vial of the nitrogen mustard mechlorethamine hydrochloride.

The contents of one 10 mg vial of mechlorethamine hydrochloride is dissolved in 50 ml of tap water. The freshly prepared solution is immediately painted on the patient's whole body surface, using gauze held in a hemostat as an applicator. The paintings are repeated until the entire 50 ml of solution has been used for the single treatment. The solution is allowed to air-dry on the skin.

The patient is instructed to take a soap and water shower or bath within three hours to remove degradation products of the nitrogen mustard from the skin. Lubricating creams or lotions are applied as required for relief of dryness or pruritus. All lubricating products are washed off before the next nitrogen mustard treatment.

A course of topical mechlorethamine hydrochloride therapy consisted of one whole body painting daily for seven days. No other specific systemic medication or radiation therapy was administered during this treatment. A rest period of at least one week between courses permitted evaluation of results. Further courses of topical nitrogen mustard were administered as indicated by the patient's response.

The first course of topical mechlorethamine solution was performed by the physician, who instructed the patient and a responsible relative in the method of mixing and applying the solution. All repeated courses were carried out by the patients' relatives at home.

Results

In the 18 months from August 1966 to February 1968, 11 patients who had recurrent mycosis fungoides following electron beam therapy were treated with courses of topical nitrogen mustard paintings (Table 1). Six of the patients were women and five were men, their ages ranging from 44 to 76 years. Two patients had received three courses of electron beam therapy, four had had two courses, and five had had one course each. The total dose per patient ranged from 600 to 3,900 rads.

All of the 11 patients with recurrences had plaques of mycosis fungoides. In addition to plaques, one woman had ulcerated plaques, one man had ulcerated plaques and tumors, and one woman had generalized erythroderma. The shortest interval between the termination of electron beam therapy and the first course of topical nitrogen mustard was six weeks and the longest was five years.

In the 11 patients, the recurrent lesions of mycosis fungoides responded to some degree to topical nitrogen mustard. Pruritus disappeared within one week and plaques and ulcers improved or disappeared in two to four weeks. There were no prolonged remissions in these patients, but they were able to control pruritus and suppress their cutaneous lesions for periods of three to fifteen months with repeated courses of topical nitrogen mustard. Three patients had excellent response, with complete disappearance of lesions. In four patients the response was good. In the remaining four patients, although pruritus was controlled, approximately half of the plaques persisted in spite

TABLE 1.—*Clinical Data on Topical Nitrogen Mustard Treatment of 11 Patients with Mycosis Fungoides*

	Electron Beam Therapy					*Topical Nitrogen Mustard Therapy*			
Case No.	*Age Yr.*	*Sex*	*Courses No.*	*Total dose Rads*	*Interval Between Electron Beam and Topical Nitrogen Mustard*	*Stage of Mycosis Fungoides*	*Courses No.*	*Duration Therapy*	*Response**
1.	57	F	3	3000 rads	2 months	plaques	14	15 months	excellent
2.	55	F	2	2725 rads	1.5 months	plaques	20	12 months	good
3.	55	M	3	3500 rads	3 months	plaques	3	12 months	fair
4.	52	M	1	2150 rads	3 months	plaques	7	7 months	good
5.	44	M	1	1600 rads	2 years	plaques	5	7 months	good
6.	76	F	2	2400 rads	6 months	plaques ulcers	4	4 months	excellent
7.	64	F	2	3900 rads	17 months	plaques	5	4 months	good
8.	70	M	1	1200 rads	28 months	plaques tumors ulcers	2	4 months	fair
9.	61	M	2	1700 rads	26 months	plaques	3	3 months	excellent
10.	60	F	1	600 rads	37 months	plaques erythroderma	2	2 months	fair
11.	54	F	1	1400 rads	5 years	plaques	2	1 month	fair

*Response: Excellent—no lesion, good—greater than 75% resolution of all lesions, Fair—50-75% resolution of all lesions.

Figure 1.—*Upper*, ulcerated plaque of mycosis fungoides before topical nitrogen mustard therapy (Case 8, Table 1). *Below*, after two courses of topical nitrogen mustard.

of repeated courses of topical nitrogen mustard. Eroded and ulcerated plaques responded best to topical nitrogen mustard (Figure 1). Tumors and erythroderma did not respond.

In three patients (Cases 2, 5, 8) topical nitrogen mustard was discontinued after 12, 7, and 4 months, respectively, and another course of 1,000 to 1,950 rads of electron beam therapy was administered. Although mechlorethamine is classified as a radiomimetic drug, it did not interfere with the effectiveness of further electron beam therapy. Conversely, electron beam therapy in doses from 600 to 3,900 rads did not decrease the patients' tolerance to topical nitrogen mustard therapy.

There was a low incidence of undesirable side-effects in the 11 patients treated with mechlorethamine paintings. No systemic toxicity or depression of leukocytes in the blood occurred. In one patient (Case 3) acute dermatitis developed. Patch tests to old and fresh mechlorethamine solution were negative, and the patient was able to tolerate future nitrogen mustard paintings. Three patients complained of pruritus during the paintings; two of them were able to continue treatment, but the third, the woman with erythroderma, refused to continue. Summaries of three cases (Cases 2, 6, 7) are presented to illustrate the response to topical nitrogen mustard.

Case 2 (as shown in Table 1). A 55-year-old white woman first noted a red scaling eruption involving the thighs in January 1964. The diagnosis of mycosis fungoides, plaque stage, was confirmed by a skin biopsy in January 1965. In 1966 she received two courses of total body electron beam therapy from 10 January to 21 February (1,225 rads) and from 2 June to 21 June (1,500 rads) for a total dose of 2,725 rads. Five weeks after the second course of electron beam therapy there was a recurrence of plaques on the flanks, arms, thighs and legs. Topical nitrogen mustard was started on 10 August. Over the next 12 months, the patient received 20 courses of topical nitrogen mustard. Each course consisted of seven consecutive daily applications with a week's rest between courses. Response was good, and it was possible to delay a third course of electron beam for 12 months. On 7 September 1967 it was noted that she had thick infiltrated plaques on the trunk and hands. A third course of electron beam therapy (1,000 rads total body) was given between 25 September and 27 October, bringing the total dose to 3,725 rads. Two weeks after electron beam therapy, there was a recurrence of plaques on the trunk. Topical nitrogen mustard was resumed on 16 November 1967 in the same manner as before for six courses. Again response was good.

Case 6 (Table 1). A 76-year-old white woman had erythematous plaques on both soles in 1949. A skin biopsy on 13 January 1966 established the diagnosis of mycosis fungoides. Two courses of total body electron beam therapy were given, 20 January to 25 February 1966 (950 rads) and 16 March to 14 April 1967 (1,450 rads) for a total dose of 2,400 rads. Four months after electron beam therapy there was a recurrence of wide-

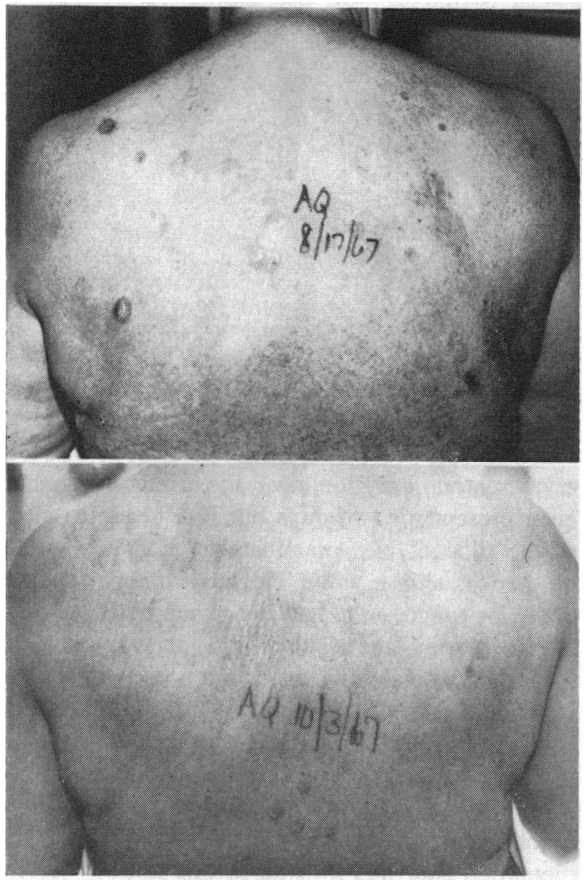

Figure 2.—Multiple plaques of mycosis fungoides before and after topically applied mechlorethamine solution (Case 7, Table 1).

spread plaques over the trunk, buttocks and thighs. Many plaques became eroded or ulcerated. On 4 October 1967 topical nitrogen mustard therapy was begun and the four courses were given. The patient bathed 15 minutes after each application because of pruritus and burning. Despite the early bathing there was an excellent response with complete clearing of lesions except for the lesions involving the left upper and lower eyelids, which were not treated with nitrogen mustard.

Case 7 (Table 1). A 64-year-old white woman began to have scaling plaques on the feet and legs in 1950. In 1963 a skin biopsy confirmed the diagnosis of mycosis fungoides. Two courses of total body electron beam therapy were given, one between 13 April and 28 May 1964 (2,400 rads), and the other 9 August to 10 September 1965 (1,500 rads) for a total dose of 3,900 rads. Plaques were noted on the legs, thighs, buttocks, back and upper extremities two months after the electron beam therapy. Topical corticosteroids of varying concentrations were used for the next 13 months. Nitrogen mustard paintings were started 21 February 1967. During the next four months the patient received five courses with a six weeks interval between the third and fourth courses. There was a 90 percent improvement (Figure 2). At the end of the four-month period, on 13 June 1967, therapy with intramuscular methotrexate was started. The patient did not respond. Topical nitrogen mustard therapy was resumed 31 August 1967, and the patient again had good response.

Discussion

Topical mechlorethamine solution had a suppressive effect in 11 patients with recurrences of mycosis fungoides. The patients had previously received up to 3,900 rads of electron beam therapy but this did not interfere with the effectiveness of topical nitrogen mustard therapy. In three patients mechlorethamine paintings did not affect tolerance to further courses of electron beam therapy, ranging up to an additional 1,950 rads in Case 8.

The pruritus in all patients was controlled by topical nitrogen mustard. As in previous reports[3] plaques and eroded or ulcerated plaques gave the best responses. Erythroderma and tumors did not respond to this treatment.

The freshly prepared dilute solution of mechlorethamine hydrochloride used in this study did not result in the contact allergic sensitization which has been reported with more concentrated solutions.[4] The immediate pruritus and discomfort which occurred in three patients during the applications were relieved by a soap and water bath as soon as the solution had dried on the skin. Early bathing, within 15 minutes, and the use of lubricating creams enabled two of the patients to continue therapy and did not diminish their response to nitrogen mustard paintings. The ease of preparation and application permitted home-use of topical nitrogen mustard therapy in our patients.

GENERIC AND TRADE NAMES OF DRUGS

Mechlorethamine hydrochloride—Mustargen®.
4-amino-N10-methylpteroylglutamic acid sodium — Methotrexate sodium®.

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